TPM3 gene

tropomyosin 3

Normal Function

The *TPM3* gene provides instructions for making a protein called slow muscle alpha (α)-tropomyosin, which is part of the tropomyosin protein family. Tropomyosin proteins regulate the tensing of muscle fibers (muscle contraction) by controlling the binding of two muscle proteins, myosin and actin. In non-muscle cells, tropomyosin proteins play a role in controlling cell shape.

Slow muscle α-tropomyosin is found in skeletal muscles, which are the muscles used for movement. Skeletal muscle is made up of two types of muscle fibers: type I (slow twitch fibers) and type II (fast twitch fibers). Slow muscle α-tropomyosin is found only in type I fibers. Type I fibers are the primary component of skeletal muscles that are resistant to fatigue. For example, muscles involved in posture, such as the neck muscles that hold the head steady, are made predominantly of type I fibers. Slow muscle α-tropomyosin helps regulate muscle contraction in type I skeletal muscle fibers.

Health Conditions Related to Genetic Changes

cap myopathy

At least two *TPM3* gene mutations have been identified in people with cap myopathy. These mutations replace the protein building block (amino acid) arginine with the amino acids cysteine or histidine at position 168 of the protein sequence, written as Arg168Cys or Arg168His (also written as R168C or R168H). The specific effects of these *TPM3* gene mutations are unclear, but researchers suggest they may interfere with normal actin-myosin binding, impairing muscle contraction and resulting in the muscle weakness that occurs in cap myopathy.

congenital fiber-type disproportion

At least 10 mutations in the *TPM3* gene have been found to cause congenital fiber-type disproportion, a disorder that causes general muscle weakness that typically does not worsen over time. *TPM3* gene mutations appear to be the most common cause of this disorder. These mutations change single amino acids in slow muscle α-tropomyosin and are thought to impair the protein's ability to interact with myosin and actin within type I skeletal muscle fibers, disrupting muscle contraction. Inefficient

muscle contraction leads to muscle weakness in people with congenital fiber-type disproportion.

nemaline myopathy

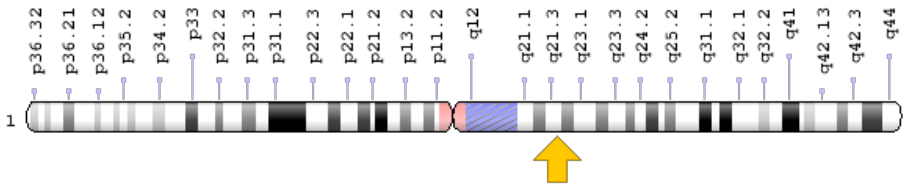
other disorders

Mutations in the *TPM3* gene are also associated with a condition called nemaline myopathy. People with nemaline myopathy typically have muscle weakness throughout their body, including the muscles of the face, neck, and limbs. When nemaline myopathy is caused by mutations in the *TPM3* gene, affected individuals typically have muscle weakness at birth or beginning in early childhood. *TPM3* gene mutations account for a small percentage of all cases of nemaline myopathy.

Chromosomal Location

Cytogenetic Location: 1q21.3, which is the long (q) arm of chromosome 1 at position 21.3

Molecular Location: base pairs 154,155,304 to 154,192,135 on chromosome 1 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- cytoskeletal tropomyosin TM30
- FLJ41118
- heat-stable cytoskeletal protein 30 kDa
- hscp30
- TM-5
- TM3
- TPM3_HUMAN
- TRK

- tropomyosin alpha-3 chain
- tropomyosin gamma

Additional Information & Resources

GeneReviews

- Congenital Fiber-Type Disproportion
  https://www.ncbi.nlm.nih.gov/books/NBK1259
- Nemaline Myopathy
  https://www.ncbi.nlm.nih.gov/books/NBK1288

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28TPM3%5BTIAB%5D%29+OR+%28tropomyosin+3%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

OMIM

- TROPOMYOSIN 3
  http://omim.org/entry/191030

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/TPM3ID225.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=TPM3%5Bgene%5D
- HGNC Gene Family: Tropomyosins
  http://www.genenames.org/cgi-bin/genefamilies/set/777
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=12012
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/7170
- UniProt
  http://www.uniprot.org/uniprot/P06753

Sources for This Summary

- Clarke NF, Kolski H, Dye DE, Lim E, Smith RL, Patel R, Fahey MC, Bellance R, Romero NB, Johnson ES, Labarre-Vila A, Monnier N, Laing NG, North KN. Mutations in TPM3 are a common cause of congenital fiber type disproportion. Ann Neurol. 2008 Mar;63(3):329-37. doi: 10.1002/ana.21308.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18300303
- De Paula AM, Franques J, Fernandez C, Monnier N, Lunardi J, Pellissier JF, Figarella-Branger D, Pouget J. A TPM3 mutation causing cap myopathy. Neuromuscul Disord. 2009 Oct;19(10):685-8. doi: 10.1016/j.nmd.2009.06.365. Epub 2009 Jun 23.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19553118
- GeneReview: Congenital Fiber-Type Disproportion
  https://www.ncbi.nlm.nih.gov/books/NBK1259
- GeneReview: Nemaline Myopathy
  https://www.ncbi.nlm.nih.gov/books/NBK1288
- Imoto C, Nonaka I. The significance of type 1 fiber atrophy (hypotrophy) in childhood neuromuscular disorders. Brain Dev. 2001 Aug;23(5):298-302.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/11504599
- Laing NG, Wilton SD, Akkari PA, Dorosz S, Boundy K, Kneebone C, Blumbergs P, White S, Watkins H, Love DR, et al. A mutation in the alpha tropomyosin gene TPM3 associated with autosomal dominant nemaline myopathy. Nat Genet. 1995 Jan;9(1):75-9. Erratum in: Nat Genet. 1995 Jun;10(2):249.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/7704029
- Lawlor MW, Dechene ET, Roumm E, Geggel AS, Moghadaszadeh B, Beggs AH. Mutations of tropomyosin 3 (TPM3) are common and associated with type 1 myofiber hypotrophy in congenital fiber type disproportion. Hum Mutat. 2010 Feb;31(2):176-83. doi: 10.1002/humu.21157.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19953533
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2815199/
- Marttila M, Lehtokari VL, Marston S, Nyman TA, Barnerias C, Beggs AH, Bertini E, Ceyhan-Birsoy O, Cintas P, Gerard M, Gilbert-Dussardier B, Hogue JS, Longman C, Eymard B, Frydman M, Kang PB, Klinge L, Kolski H, Lochmüller H, Magy L, Manel V, Mayer M, Mercuri E, North KN, Peudenier-Robert S, Pihko H, Probst FJ, Reisin R, Stewart W, Taratuto AL, de Visser M, Wilichowski E, Winer J, Nowak K, Laing NG, Winder TL, Monnier N, Clarke NF, Pelin K, Grönholm M, Wallgren-Pettersson C. Mutation update and genotype-phenotype correlations of novel and previously described mutations in TPM2 and TPM3 causing congenital myopathies. Hum Mutat. 2014 Jul;35(7):779-90. doi: 10.1002/humu.22554. Epub 2014 May 1.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/24692096
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4200603/
- Ochala J. Thin filament proteins mutations associated with skeletal myopathies: defective regulation of muscle contraction. J Mol Med (Berl). 2008 Nov;86(11):1197-204. doi: 10.1007/s00109-008-0380-9. Epub 2008 Jun 24. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18574571

- OMIM: TROPOMYOSIN 3
  http://omim.org/entry/191030
- Waddell LB, Kreissl M, Kornberg A, Kennedy P, McLean C, Labarre-Vila A, Monnier N, North KN, Clarke NF. Evidence for a dominant negative disease mechanism in cap myopathy due to TPM3. Neuromuscul Disord. 2010 Jul;20(7):464-6. doi: 10.1016/j.nmd.2010.05.012. Epub 2010 Jun 15.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20554445

Reprinted from Genetics Home Reference:
https://ghr.nlm.nih.gov/gene/TPM3

Reviewed: May 2016
Published: March 21, 2017

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services